20. MacCarty, W. C.: The histogenesis of cancer (carcinoma) of the breast and its clinical significance, Surg., Gynec. and Obst., 1913, xvii, 441–450.

21. MacCarty, W. C.: Clinical suggestions based upon a study of primary, secondary (carcinoma?) and tertiary or migratory (carcinoma) epithelial hyperplasia in the breast, Surg., Gynec. and Obst., 1914, xviii, 284–289.

22. MacCarty, W. C.: New facts and their clinical significance concerning cancer. Surg., Gynec. and Obst., 1915, xxi, 6–8.

23. MacCarty, W. C.: Precancerous conditions, Jour. Iowa St. Med. Soc., 1914, iv, 1–11.

24. MacCarty, W. C.: A new classification of neoplasms and its clinical value. Am. Jour. Med. Sc., 1906, cli, 799–806.

25. Mallory, F. B.: Principles of pathologic histology, Philadelphia, Saunders, 1914, 677 pp.

26. Morgan, T. H.: Regeneration, New York, Macmillan, 1901.

27. Pander: Quoted by Morgan.

28. Ribbert, M. W. H.: Geschwülstlehre, Bonn, Cohen, 1904–6.

29. See text-book of pathology.

30. Wolff: Quoted by Morgan.

31. Ziegler, E.: Text-book of special pathological anatomy, New York, Macmillan, 1898, 2 vs.

THE PROGNOSTIC VALUE OF THE CREATININE OF THE BLOOD IN NEPHRITIS.*

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Attention has been called in several communications[1] to the prognostic value of the creatinine content of the blood in cases of advanced nephritis. We now have a much larger series of cases, indicating the value of this test, and it has been thought worth while to briefly summarize all our data on this subject.

In our studies on nitrogen retention it was soon noted that the creatinine of the blood was appreciably increased only after considerable retention of urea had already taken place and the nephritis was rather far advanced. It was further observed that those cases in which the creatinine had risen above 5 mg. per 100 c.c. of blood rarely showed any marked improvement, and almost invariably died within a comparatively limited time. On the other hand a number of cases were encountered in which there was a marked retention of urea, but in which the creatinine was below this figure. In many of these cases improvement took place.

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* Read in part before the Society for Experimental Biology and Medicine, December 18, 1918.

[1] Myers and Lough: Arch. Int. Med., 1915, xvi, 536; Chace and Myers: Jour. Am. Med. Assn., 1916, lxvii, 929.

Theoretically, the amount of the increase of the creatinine of the blood should be a safer index of the decrease in the permeability of the kidney than the urea, for the reason that creatinine on a meat-free diet is entirely endogenous in origin and its formation (and elimination normally) very constant. Urea, on the other hand, is largely exogenous under normal conditions and its formation consequently subject to greater fluctuation. For this reason it must be evident that a lowered nitrogen intake may reduce the work of the kidney in eliminating urea, but cannot affect the creatinine to any extent. Apparently the kidney is never able to overcome the handicap of a high creatinine accumulation. It would seem that creatinine, being almost exclusively of endogenous origin, furnishes a most satisfactory criterion as to the deficiency in the excretory power of the kidneys and a most reliable means of following the terminal course of the disease, though it should be noted that urea, being largely of exogenous origin, is more readily influenced by dietary changes, and therefore constitutes a more sensitive index of the response to treatment.

The view that uremic symptoms are due directly to retained urea, uric acid or creatinine has now long been regarded untenable, although the recent work of Hewlett, Gilbert and Wickett[2] is of interest in this connection. They found that the administration to normal subjects of sufficient urea to produce a blood concentration of 150 mg. per 100 c.c. (70 mg. of urea nitrogen) resulted in symptoms of bodily and mental asthenia. They state: "This by no means excludes the possibility that other substances may play a rôle in producing the symptoms of this type of uremia, and, indeed, the fact that animals die only when extraordinary doses of urea are administered suggests that the fatal outcome of asthenic uremia in man may be due to other substances than urea." That urea and uric acid may break up in the body into anything more toxic seems improbable, but the possibility that retained creatinine may give rise to the toxic methylguanidine lends further interest to creatinine in this connection. In 1912 W. F. Koch[3] isolated methylguanidine from the urine of animals dying from parathyroid tetany. More recently, Paton and his co-workers[4] have demonstrated that there is a marked increase in the amount of guanidine and methylguanidine in the blood and urine of dogs after the removal of the parathyroids and in the urine of children suffering from idiopathic tetany. Foster[5] has been able to isolate a very toxic substance from uremic blood in the form of a gold salt. This substance when injected into animals produces symptoms similar to those noted in uremia. Although Foster did not obtain sufficient of this compound to identify it, it is significant that guanidine compounds form very characteristic gold salts. These observations lend support to the view that the retention of creatinine may possess special significance in uremia. This topic is one upon which we are endeavoring to obtain further information.

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[2] Arch. Int. Med., 1916, xviii, 636.

[3] Jour. Biol. Chem., 1912, xii, 313.

[4] Quart. Jour. Exper. Physiol., 1917, x, 203-382.

[5] Tr. Assn. Am. Phys., 1915, xxx, 305.

As the result of recent studies on acidosis,[6] it is now recognized that nearly all advanced cases of nephritis show a considerable degree of acidosis,[7] probably due to a retention of (acid) phosphate.[8] In this connection it is of interest that Watanabe[9] has found that the administration of guanidine to animals induces a condition of severe acidosis with the retention of phosphate and a decrease of calcium in the blood. It may be mentioned that a few unpublished analyses which we have made on terminal cases of nephritis show a marked decrease in the calcium content of the blood.

Turning to the more practical side of this question, it is our opinion that in these advanced cases of nephritis the blood creatinine furnishes a more reliable prognosis than any other test that we possess. Our observations in support of this statement are furnished in the tables below. Figures are likewise included for urea and phenolsulphonephthalein. Although, as a rule, several blood analyses were carried out during the course of the disease, only one set has been recorded in Table I. This has generally been the last observation obtained before death or previous to the patient's leaving the hospital.

METHODS EMPLOYED. Inasmuch as there has recently been some discussion of the absolute accuracy of the creatinine estimation in blood, it may be well to make a few remarks regarding this determination. Prior to the publication by Folin of his method for this determination we had already carried out a few estimations of this substance in blood,[10] utilizing suggestions made by Shaffer and Reinoso[11] several years previously for the estimation of creatinine in dilute solutions. With the publication of Folin's paper[12] we adopted his method for the most part, except that we still continued to carry out the preliminary dilution of the blood with water rather than picric acid solution, for the reason that we regarded this the preferable way of analyzing the whole blood. Furthermore, we have always combined the creatinine and blood-sugar[13] estimations, as this is also a suitable preliminary step in the case of the sugar estimation.

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[6] Van Slyke and Cullen: Jour. Biol. Chem., 1917, xxx, 289; Van Slyke: ibid., p. 347.

[7] Whitney: Arch. Int. Med., 1917, xx, 931.

[8] Marriott and Howland: Ibid., 1916, xviii, 708.

[9] Watanabe: Jour. Biol. Chem., 1918, xxxvi, 531.

[10] Myers and Fine: Proc. Soc. Exp. Biol. Med., 1914, xi, 132, and Chemical Composition of the Blood in Health and Disease, reprinted from The Post-Graduate, 1914–15, p. 19.

[11] Jour. Biol. Chem., 1910, vii, proceedings, p. xxx.

[12] Ibid., 1914, xvii, 475.

[13] Myers and Bailey: Ibid., 1916, xxiv, 147.

Our technic has been as follows: To 20 c.c. of distilled water in a 50 c.c. centrifuge tube are added 5 c.c. of the well-mixed oxalated blood. This is then stirred with a glass rod until the blood is thoroughly hemolyzed, after which about 1 gram of dry picric acid (sufficient to completely precipitate the proteins and render the solution saturated) is added. The mixture is thoroughly stirred until it is uniformly yellow and then at intervals for twenty to thirty minutes, after which it is centrifuged and filtered. Sufficient filtrate is obtained for the estimation of both the creatinine and the sugar. To 10 c.c. of this filtrate is added 0.5 c.c. of 10 per cent. sodium hydroxide and a similar amount of alkali added to each of three standards (10 c.c. of standard creatinine in saturated picric acid, containing 0.3, 0.5 and 1.0 mg. creatinine to 100 c.c. of picric acid). Pure creatinine is readily prepared by the admirable method of Benedict.[14] A standard solution of creatinine, 1 mg. to 1 c.c., is kept in 0.1 N hydrochloric acid, and from this the various solutions are prepared with saturated picric-acid solution. A standard is selected which approximates the color intensity of the unknown, the prism being set at the 10 or 15 mm. mark. With bloods showing over 5 mg. of creatinine it has been customary to further dilute the blood filtrate with saturated picric-acid solution, so that the color when developed would match, *e. g.*, between the 7 and 13 mm. mark when the standard was set at 10. Originally we allowed ten minutes for the development of the color, but owing to the observations of Hunter and Campbell[15] this has been reduced to eight minutes. We have experienced comparatively little difficulty with color-forming substances in the picric acid, although some of our picric acid has been purified by the method of Folin and Doisy.[16]

In a paper dealing with the creatinine content of the blood of different animals, Wilson and Plass[17] pointed out that the results were higher in whole blood than in plasma. They also found that using alumina cream as the protein precipitant, a method which we had previously employed in determining creatinine in muscle,[18] slightly lower results were obtained than when the Folin method was employed. Hunter and Campbell[19] have recently made a more extensive study of this question. Although they originally made their creatinine estimations on laked blood, following our suggestion, they have recently obtained data which tend to show that these results are somewhat too high (particularly in normal blood), owing to an interference in the color development on the part of some constituent in the corpuscles. With plasma, however, the results appear to be approximately correct. Greenwald and McGuire[20] have likewise studied this question. They employed two methods of precipitating the blood proteins aside from picric acid, viz., colloidal iron and trichloracetic acid. Their results with these methods of precipitation were slightly lower than with the Folin method, although not uniformly so. In carrying out the picric-acid precipitation they followed our suggestion in laking the blood first, but regarded shaking necessary to render the solution saturated. In our hands it has been found possible to obtain a much more homogeneous mixture with the aid of a stirring rod than with shaking alone. Denis[21] has recently suggested still another method of precipitating the proteins. She employs metaphosphoric acid apparently to very excellent advantage, inasmuch as she has been able to utilize the preliminary precipitation for an apparently satisfactory estimation of creatine as well. Her results for creatinine, though slightly lower, differ but little from those obtained by the Folin method on normal blood.

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[14] Myers and Bailey: Jour. Biol. Chem., 1914, xviii, 183.

[15] Ibid., 1917, xxxii, 195.

[16] Ibid., 1916-17, xxviii, 349.

[17] Ibid., 1918, xxxv, 513.

[18] Myers and Fine: Ibid., 1914, xvii, 65.

[19] Loc. cit.

We have taken occasion to compare the creatinine content of the blood with that of the plasma in cases of marked retention, and have found the figures in the plasma about 10 per cent. lower than in the whole blood, a difference which we scarcely believe to be entirely due to the intervening substance in the corpuscles.[22] Although, as Hunter and Campbell have pointed out, the creatinine estimation in normal blood is probably more accurate in plasma than in whole blood, the absolute accuracy of the estimation in whole blood is much greater with pathological than normal values, *i. e.*, the accuracy increases with its clinical importance.

The urea estimations were made by a modified Marshall-Van Slyke method, essentially as described by Myers and Fine.[23] The enzyme used is that derived from the jack bean. The Nessler solution employed at present is from a very satisfactory formula furnished us by Drs. Benedict and Bock, which contains 100 grams of mercuric iodide, 70 grams of potassium iodide and 100 grams of sodium hydroxide per liter of solution. The phthalein injections were made intramuscularly in practically all cases. The CO_2 combining power recorded on a number of the cases under the heading of remarks was made according to the Van Slyke method.[24] In the last three columns of Table I are recorded the length of time under observation and present condition, together with a few remarks pertinent to the history of the individual cases. Unless otherwise noted the clinical diagnosis was chronic interstitial nephritis.

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[20] Myers and Fine: Jour. Biol. Chem., 1918, xxxiv, 103.

[21] Ibid., 1918, xxxv, 513.

[22] Hunter and Campbell: Jour. Biol. Chem., 1917, xxxii, 195.

[23] Arch. Int. Med., 1916, xvii, 570.

[24] Cullen and Van Slyke: Jour. Biol. Chem., 1917, xxx, 289; Van Slyke: Ibid., 347.

DISCUSSION. The 100 cases[25] recorded in Table I would seem to be a sufficiently large series to enable one to arrive at fairly definite conclusions. In an earlier communication by Myers and Lough,[26] dealing with the prognostic value of the creatinine of the blood in nephritis, the statement was made: "Creatinine values from 2.5 to 3 mg. may be viewed with suspicion; figures from 3 to 5 mg. regarded as decidedly unfavorable, while over 5 mg. probably indicate an early fatal termination." Although the great majority of cases without kidney involvement show creatinine figures on the whole blood below 2.5 mg. per 100 c.c., occasionally figures as high as 3.5 mg. are encountered that are not readily explained. It may be noted, however, that a slight retention of creatinine (figures between 3 and 4 mg.) occurs in syphilis, certain heart conditions, and in some advanced cases of diabetes. Creatinine figures above 3.5 mg. are almost invariably accompanied by an appreciable urea retention and this is generally true of those above 3 mg. Many of the cases below 4 mg. show improvement, but with over 4 mg. the reverse is the case. It would appear from this that an appreciable retention of creatinine, *i. e.*, over 4 mg., does not occur until the activity of the kidneys is greatly impaired.

As will be noted in Table I, the 100 cases are arranged in the order of the magnitude of the blood creatinine. The series includes all cases with over 5 mg. creatinine which have come under our observation since March, 1914, with the exception of 3 patients whom we have been unable to trace and who are presumably dead. It will be observed that the first 73 cases in the series are all dead, with the exception of Case 59 (P. H.), whose condition remains essentially unchanged at the present writing. Sixty of these first 73 cases died within two months after they came under our observation, although the remainder lived for periods varying from three months to one year. It may be of interest to note that Case I (W. F.) died from bichloride poisoning while Cases 52 (H. B.) and 64 (E. H.) suffered from double polycystic kidney. Even among the first 73 cases of the series there were many who were able to be up and about and some who showed considerable clinical improvement. It was in these cases that we believe the blood creatinine gave us a particularly good prognostic insight into the true nature of the condition.

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[25] Most of these cases were patients in the medical wards of the hospital, although some were patients in the urological and surgical wards. We are especially indebted to Drs. Chace, Kast and Halsey of the Medical Department, Dr. Squier of the Urological Department, and Drs. Erdmann and Lloyd of the Surgical Department for their coöperation in helping us to obtain these data. In following the different cases during the past five years, we are indebted to the following former members of the house staff, Drs. Lough, Nacey, Donaldson and Costen.

[26] Loc. cit.

TABLE I.—THE PROGNOSTIC VALUE OF THE CREATININE OF THE BLOOD IN NEPHRITIS.*

Case.	Date.	Age.	Sex.	Blood analyses.		Phthalein, two-hour output, per cent.	Time under observation.	Present condition.	Remarks.
				Creatinine. mg. to 100 c.c.	Urea N. mg. to 100 c.c.				
1. W. F.	Nov. 20, 1914	25	M.	33.3	240	. . .	1 mo.	Dead	Case of bichloride poisoning; died 16 days after this observation; uremic symptoms appeared one week previous to death, although the creatinine had then fallen to 14.8 mg.
2. E. M.	Dec. 21, 1915	39	M.	28.6	186	0	3 wks.	"	Able to be up and about and did not realize the seriousness of his condition when first admitted three weeks before this examination, although his creatinine was then 17.5 mg.; died Dec. 25, his CO_2 combining power having then fallen to the low figure of 12, despite treatment.
3. A. C.	Oct. 11, 1917	53	M.	22.5	106	0	2 wks.	"	Marked dyspnea, CO_2 on Oct. 15, 25; died nine days after this examination.
4. S. H.	June 25, 1915	37	M.	22.2	262	0	5 wks.	"	Admitted to hospital on May 8, complaining of stomach trouble; after phlebotomy on June 26 patient was much brighter and pulse better; died on June 28.
5. T. D.	Mar. 23, 1915	34	M.	20.5	152	4 to 0	2 mos.	"	Dizziness; retinal hemorrhages; in hospital two months; died Mar. 23.
6. I. D.	Jan. 3, 1915	17	F.	20.0	209	0	1 mo.	"	Moderate dilatation of heart; died Jan. 4.
7. P. J.	Feb. 14, 1916	43	M.	20.0	162	0	4 days	"	CO_2 combining power on this date 43; extreme dyspnea; bilateral decapsulation; died about two and a half hours after operation.
8. L. R.	Aug. 2, 1916	25	F.	20.0	108	Trace	3 wks.	"	Generalized edema; also lobar pneumonia; CO_2 36 Aug. 4, date of death.
9. E. D.	June 26, 1917	53	F.	19.8	114	0	2 wks.	"	Marked dyspnea; CO_2 on admission 27; after rectal administration of 2 per cent. $NaHCO_3$ June 26 the CO_2 rose to 76; died three days later in uremia.
10. N. W.	Sept. 4, 1918	19	F.	19.2	164	0	2 wks.	"	Admitted Aug. 29, CO_2 Sept. 4, 31; removed against advice Sept. 12; died at home in convulsions the following day.

11. E. L.	Mar. 28, 1916	20	F.	18.9	141	0	2 wks.	"	Clinical diagnosis, acute parenchymatous nephritis; CO₂ this date 46; died the following day.
12. R. A.	Nov. 6, 1916	30	F.	18.7	68	...	1 wk.	"	Acute hemorrhagic nephritis, with complete suppression of urine; bilateral decapsulation Nov. 4; CO₂ then 38; lived three days after operation, two specimens of urine being obtained.
13. M. M.	May 19, 1916	40	F.	18.3	246	...	2 days	"	Admitted May 18 and died two days later; also chronic endocarditis.
14. M. B.	Jan. 3, 1919	48	M.	18.1	172	...	1 wk.	"	Admitted Dec. 29; discharged unimproved Jan. 4; died at home next day.
15. E. P.	Dec. 12, 1916	34	F.	17.6	85	0	2 wks.	"	Admitted Dec. 6, also purpura hemorrhagica; CO₂ Dec. 12, 32; left hospital against advice Dec. 14 and died at home Dec. 19.
16. E. C.	April 11, 1915	50	F.	16.7	236	0	2 days	"	Died this date, two days after admission.
17. W. O'C.	Mar. 8, 1914	33	M.	16.6	182	Trace	7 wks.	"	Marked cyanosis and dyspnea; died the day following this observation.
18. M. K.	May 13, 1914	42	M.	14.7	170	...	3 wks.	"	Diagnosis, chronic diffuse nephritis; marked edema and cyanosis; coma; double decapsulation this date; patient died during operation.
19. K. K.	Mar. 26, 1915	39	F.	14.7	148	0	1 wk.	"	Considerable cardiac hypertrophy; died Mar. 27, one week after admission.
20. J. H.	May 16, 1916	29	M.	14.7	77	...	2 wks.	"	Admitted May 1; died May 18.
21. W. C.	Mar. 20, 1917	24	M.	14.5	123	Trace	2 wks.	"	Bilateral decapsulation Mar. 22, died five days later.
22. M. P.	Jan. 3, 1917	25	M.	14.4	141	0	2 wks.	"	Albuminuric retinitis with almost complete loss of vision. CO₂ 31 Dec. 26, but administration of bicarbonate brought this up. It was 44 Jan. 5, the date of death.
23. A. M.	Sept. 25, 1918	44	M.	13.5	147	0	2 mos.	"	Admitted Sept. 16 and died Nov. 18; chief complaint on admission, weakness and loss of appetite; CO₂ 32 on admission.
24. E. P.	Mar. 1, 1916	40	F.	12.7	116	0 to 1	3 mos.	"	Died Mar. 25, three months after first observation and six weeks after being removed from hospital against advice; retinal hemorrhages.

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* Strictly normal values for the creatinine of the blood may be given as 1 to 2 mg. per 100 c.c., urea N, 12 to 15 mg., uric acid 2 to 3 mg., sugar 0.09 to 0.12 per cent., and CO_2 combining power 50 to 75 c.c. per 100. Unless patients are under specially controlled conditions, deductions are not drawn from individual figures which do not exceed 3.5 mg. creatinine, 20 mg. urea N, 4.5 uric acid, 0.15 per cent. sugar or CO_2 combining power that is below 45 c.c.

TABLE I.—THE PROGNOSTIC VALUE OF THE CREATININE OF THE BLOOD IN NEPHRITIS—*continued.*

Case.	Date.	Age.	Sex.	Blood analyses.		Phthalein, two-hour output, per cent.	Time under observation.	Present condition.	Remarks.
				Creatinine. mg. to 100 c.c.	Urea N. mg. to 100 c.c.				
25. A. N.	Mar. 22, 1918	27	F.	12.6	110	0	2⅓ mos.	Dead	Discharged Mar. 30; clinically improved; albuminuric retinitis, readmitted Apr. 27; no change in blood; died May 25; May 22, urea N 148; creatinine 17 and CO_2 combining power 12.
26. A. L.	July 25, 1918	52	F.	12.6	78	. . .	5 days	"	Clinical diagnosis, chronic diffuse nephritis; complained of weakness and edema for six months; CO_2 combining power 32; admitted July 24; died July 29.
27. M. N.	June 30, 1916	46	M.	12.5	210	0	3 mos.	"	Patient admitted Apr. 3, but left hospital against advice May 15; condition slightly improved; readmitted June 19; died July 2.
28. W. W.	Feb. 23, 1916	30	M.	12.5	76	0	5 mos.	"	Also fibroid phthisis; admitted Feb. 7, discharged improved May 1; improvement coincident with rise in CO_2 combining power; returned to Ireland; died there in July.
29. W. S.	Jan. 30, 1917	. .	M.	12.5	97	. . .	1 wk.	"	Patient brought to laboratory by clinic physician, who remonstrated at our prognosis; patient died a week later
30. J. B.	Jan. 9, 1917	34	M.	12.5	110	3 to 10	11 mos.	"	Admitted Dec. 19, 1916; swelling of feet, hands and face one year; headaches three weeks; heavy drinker; discharged clinically improved June 9, with a urea N of 33.5 and a creatinine of 6.7 mg.; died Nov. 7, 1917.
31. J. M.	Sept. 11, 1918	38	M.	12.2	72	0	6 wks.	"	In hospital Aug. 29 to Sept. 23; readmitted Oct. 2; died Oct. 14.
32. S. B.	Sept. 17, 1917	51	F.	11.6	57	0	1 wk.	"	Admitted complaining of acute gastritis Aug. 15; left hospital unimproved against advice Aug. 17; died shortly after being taken home.
33. F. R.	April 2, 1917	32	M.	11.5	102	0	1 wk.	"	Chronic diffuse nephritis and uremia; admitted Apr. 1; died Apr. 8; CO_2 combining power, Apr. 2, 39.
34. M. O.	May 28, 1915	8	F.	11.1	90	0	6 wks.	"	Admitted May 11; double decapsulation of kidneys May 13; died in uremia June 29.

35. H. K.	July 27, 1915	41	M.	11.1	91	0 to 3	6 wks.	“	Admitted July 24; removed against advice Aug. 25; died about two weeks later; mitral insufficiency; pleural effusion.
36. H. E.	Jan. 26, 1917	36	M.	11.1	139	4	1 wk.	“	Admitted Jan. 19; died Jan. 27, the day following this observation.
37. J. W.	April 14, 1915	34	M.	11.0	144	3 to 1	2 mos.	“	Slight cardiac hypertrophy; marked neuroretinitis; died April 16, two months after admission; showed marked clinical improvement, and said he felt perfectly well until three days before death.
38. A. D.	Oct. 13, 1916	30	M.	11.0	97	. . .	3 days	“	Clinical diagnosis, acute parenchymatous nephritis; admitted Oct. 13; died Oct. 16; CO_2 combining power 35 Oct. 13.
39. J. D.	July 16, 1915	33	M.	10.7	78	0 to 6	2 mos.	“	Admitted June 5; discharged improved July 17; died about two weeks later.
40. J. M.	Feb. 15, 1918	17	F.	10.2	307	0	1 wk.	“	Admitted Jan. 29; died eight days after this test Feb. 13; CO_2 combining power 30 Feb. 1.
41. C. G.	Sept. 24, 1915	26	F.	10.0	112	0	3 wks.	“	Malignant endocarditis with terminal uremia; admitted Sept. 7; died Sept. 24, the date of this examination.
42. J. G.	May 14, 1917	30	F.	9.8	62	0	7 mos.	“	In hospital Nov. 2 to Dec. 19, 1916, and Dec. 26 to Feb. 1, 1917; chief complaint on second admission, swelling of legs; 0 phthalein on Jan. 8; died at home June 1.
43. J. B.	Oct. 5, 1918	78	M.	9.8	60	Trace	2 mos.	“	Also hypertrophied prostate and cystitis; in hospital Sept. 28 to Oct. 29; CO_2 31 Oct. 23; died Dec. 7 at home.
44. Z. F.	June 26, 1917	64	M.	9.7	70	12	5 mos.	“	Arteriosclerosis with hypertension, admitted June 11; discharged improved June 29; died about four months after leaving hospital.
45. P. L.	Mar. 7, 1918	30	M.	9.5	140	0	2 mos.	“	Admitted Feb. 28; also empyema; discharged improved Mar. 21; died about Apr. 22.
46. A. R.	June 21, 1918	51	F.	9.5	89	. . .	6 mos.	“	Outside patient; died Dec. 15.
47. J. S.	May 4, 1917	69	M.	9.4	89	. . .	2 wks.	“	Also prostatic obstruction; died about two weeks after this observation.
48. L.	July 21, 1916	. .	M.	9.2	54	. . .	2 days	“	Private case outside hospital; syphilis; died on following day.
49. S. W.	Jan. 14, 1916	56	M.	9.1	224	0	2 wks.	“	Bacteremia; suppression of urine; lobar pneumonia; died two days after this observation.
50. I. H.	Nov. 16, 1917	43	F.	8.8	55	20-5	3 wks.	“	Admitted Oct. 26, complaining of pains in back and edema of feet; removed against advice Nov. 18; died two hours after leaving hospital.

TABLE I.—THE PROGNOSTIC VALUE OF THE CREATININE OF THE BLOOD IN NEPHRITIS—*continued*.

Case.	Date.	Age.	Sex.	Blood analyses.		Phthalein, two-hour output, per cent.	Time under observation.	Present condition.	Remarks.
				Creatinine. mg. to 100 c.c.	Urea N.				
51. V. A.	Feb. 15, 1916	27	M.	8.3	59	6–4–2	3 mos.	Dead	In hospital one week; died at home about three months later.
52. H. B.	Jan. 22, 1917	40	M.	8.3	75	...	1 yr.	"	Double polycystic kidney; admitted Jan. 22; nephrotomy on one side Jan. 24; left hospital improved, but died after an attack of pain on opposite side a year later.
53. J. W.	May 15, 1917	57	M.	8.2	95	...	2 wks.	"	Carcinoma of bladder; died in coma three days after this examination.
54. A. J.	Mar. 11, 1918	20	M.	8.0	131	...	5 days	"	Admitted Mar. 10; removed against advice Mar. 12; died three days later; possible bichloride poisoning.
55. J. S.	Nov. 23, 1914	50	M.	7.4	81	...	1 day	"	Slight edema of lower extremities; suppression of urine; died on day of admission.
56. R. W.	July 19, 1918	67	M.	7.1	82	0	3 mos.	"	Admitted July 18; blindness of right eye; shortness of breath for two years past; arteriosclerosis; retinal thrombosis; discharged improved Aug. 2; CO_2 26 July 19 and 42 Aug. 2; died at home Oct. 11.
57. W. G.	July 13, 1914	8	M.	7.0	94	5	2 mos.	"	Acute nephritis of mixed type with uremia and edema; purpura hemorrhagica; died shortly after being removed from hospital against advice.
58. J. B.	May 3, 1918	46	M.	7.0	78	0	1 wk.	"	Died in coma six days after this analysis; at necropsy found hypertrophied heart and kidneys of arteriosclerotic type.
59. P. H.	June 28, 1918	64	M.	7.0	128	...	7 mos.	Unchanged	Clinical diagnosis, chronic parenchymatous nephritis and hypertrophied prostate; no operation; CO_2 on this date 45; in hospital June 21 to July 27; Jan. 27 condition unchanged although nitrogen retention had dropped; creatinine 4.4 and urea N 43.
60. O. P.	May 4, 1918	60	M.	6.9	97	...	2 wks.	Dead	Died apparently as a result of nephritic acidosis five days after this analysis; CO_2 Apr. 27, 32; operation for carcinoma of bladder four months previously; death not due to metastasis, as patient was not cachectic.

61. T. N.	Mar. 27, 1917	43	M.	6.8	105	0	2 mos.	"	Admitted Mar. 18 and removed against advice Mar. 30; previously in hospital but discharged Feb. 22; died shortly after being removed from hospital.
62. B. M.	June 26, 1918	47	M.	6.8	77	...	5 days	"	Acute nephritis; admitted June 22 and died June 27.
63. E. W.	Feb. 15, 1916	69	M.	6.7	104	...	2 wks.	"	Admitted Feb. 5; Wassermann positive; hypertrophied prostate; prostatectomy under novocaine; died Feb. 20.
64. E. H.	Aug. 14, 1917	20	F.	6.7	38	Trace	3 wks.	"	Double polycystic kidney; admitted Aug. 8; died Aug. 30, sixteen days after this observation.
65. J. H.	Feb. 7, 1917	61	M.	6.6	133	...	2 wks.	"	Admitted Jan. 24; died Feb. 8.
66. B. D.	July 18, 1918	70	M.	6.6	219	...	3 wks.	"	Admitted June 25; blood, June 27, creatinine 1.9 mg. and urea N 18; phthalein 85 per cent.; prostatectomy; patient did poorly for no apparent reason; died July 18.
67. S. G.	Nov. 8, 1917	53	M.	6.4	26	11–23	8 mos.	"	Admitted Oct. 20; discharged improved Dec. 7; very poor condition April 19, 1918; died in June.
68. F. A.	Sept. 5, 1916	53	M.	6.3	97	...	1 wk.	"	Clinical diagnosis, chronic diffuse nephritis; admitted Aug. 30; died Sept. 5.
69. J. McC.	Dec. 31, 1915	56	M.	6.2	53	2–8–7–10	8 mos.	"	Clinical diagnosis, chronic parenchymatous nephritis; admitted Dec. 27; discharged improved; CO_2 on admission 20; clinical improvement followed rise to normal; died from pneumonia Aug. 24.
70. C. L.	June 22, 1917	46	M.	6.2	39	23–10–26	5 wks.	"	Clinical diagnosis, chronic diffuse nephritis; uremia; admitted May 16; died June 24, two days after last blood examination.
71. B. S.	Oct. 18, 1918	52	M.	6.2	70	7 to Tr.	4 mos.	"	Chronic diffuse nephritis; marked edema at first; complained of headache and failing vision; carcinoma of sigmoid found at autopsy; in hospital Aug. 23 to Sept. 13 and Oct. 2 to Nov. 12.
72. A. F.	Feb. 18, 1916	45	M.	6.1	114	9	2 wks.	"	Multiple calculi of left kidney, nephrectomy, calculus of right kidney; nephrotomy; in hospital two weeks; died day after this observation.
73. N. W.	Nov. 20, 1916	21	F.	6.1	72	...	2 days	"	Also chronic polyarthritis deformans; sick four weeks; admitted Nov. 19; died next day.
74. F. F.	Dec. 18, 1917	8	M.	6.1	106	16–42–57	1 yr.	Recovered	Admitted Dec. 17 complaining of suppression of urine and edema of face; discharged improved Jan. 17; apparently recovered at present time.
75. J. C.	April 8, 1917	60	M.	6.1	41	10–7–9	21 mos.	Unchanged	Clinical diagnosis, chronic diffuse nephritis; admitted April 23; discharged improved June 10; readmitted a year later; Jan. 19, 1919, creatinine 4.3 mg. and urea N 64.

TABLE I.—THE PROGNOSTIC VALUE OF THE CREATININE OF THE BLOOD IN NEPHRITIS—*continued.*

Case.	Date.	Age.	Sex.	Blood analyses.		Phthalein, two-hour output, per cent.	Time under observation.	Present condition.	Remarks.
				Creatinine. mg. to 100 c.c.	Urea N. mg. to 100 c.c.				
76. M. R.	Dec. 3, 1915	56	M.	6.0	52	3–6	3 mos.	Dead	Endocarditis; chronic renal calculus (right); admitted Dec. 21; left hospital improved Mar. 9; died shortly after returning home.
77. H. C.	May 27, 1918	59	M.	6.0	169	. . .	3 wks.	"	Also carcinoma of bladder; CO_2 40, operated on July 16; in hospital July 14 to Aug. 2.
78. H. G.	May 29, 1917	21	M.	5.6	70	17–24–35	1½ yrs.	Recovered	Admitted May 2; discharged improved June 10; June 15 creatinine 2.5 and urea N 23; apparently well for more than a year past; in army at present time.
79. M. M.	June 19, 1917	50	F.	5.5	62	15–10–8	3 mos.	Dead	Also marked hypertension and endocarditis; first admitted on June 14; discharged improved Aug. 4; July 27, creatinine 2.5 and urea N 20 mg.; readmitted Aug. 9; died Sept. 16.
80. A. F.	Aug. 21, 1918	12	F.	5.4	42	25 to Tr.	4 mos.	"	In hospital for removal of adenoids May, 1916; urine then showed albumin and casts; again admitted on Aug. 19, 1918, complaining of headaches, convulsions and blindness; discharged Sept. 18, feeling fairly well; readmitted Nov. 18; Dec. 11, creatinine 13.6 and urea N 217; died Dec. 14.
81. F. Q.	May 9, 1918	53	F.	5.3	100	6	4 mos.	"	Removed against advice; died Sept. 14 in convulsions; blind three days before death.
82. E. E.	Jan. 19, 1915	30	F.	5.3	100	10	1 mo.	"	Wassermann 4+; generalized edema; died on this date, one month after admission.
83. R. McC.	Sept. 18, 1918	62	M.	5.3	25	0	2 mos.	Improved	Admitted Oct. 16; prostatectomy; blood Nov. 8 showed a creatinine of 4.9 and urea N of 32; recovered from operation and left hospital Nov. 19; well on Dec. 25.
84. A. D.	Sept. 27, 1915	29	F.	5.2	65	. . .	1 wk.	Dead	Bichloride poisoning.
85. E. H.	Sept. 14, 1917	21	M.	5.1	42	15–21	5 mos.	"	Admitted Dec. 7 complaining of convulsions following headache; discharged improved Dec. 20; died at Scotia, N. Y., May 3.

86. T. B.	Feb. 1, 1918	46	M.	5.0	41	31-21-10	6 mos.	Improved	Osteomyelitis of both femora; observation Dec. 10 t. 18, 1917, creatinine 2.5 and urea N 19 on Dec. 11 readmitted Jan. 9, discharged improved Feb. 20; still improved in August.
87. J. F.	July 17, 1918	65	M.	5.0	48	. . .	6 mos.	"	Admitted to hospital July 15; fibroid prostate removed July 25; left hospital Aug. 20; complete recovery from operation; Jan. 24 creatinine 2.4 and urea N 22.
88. E. H.	July 26, 1918	39	M.	5.0	42	. . .	1 wk.	Dead	Malignancy of bladder; CO_2 combining power 40.
89. T. K.	Mar. 7, 1916	62	M.	4.9	53	. . .	4 mos.	"	Hypertrophied prostate; prostatectomy; died three and a half months later from lobar pneumonia; nitrogen retention still existed.
90. L. P.	Jan. 6, 1915	57	M.	4.8	80	0-38-10	1 yr.	"	Admitted Jan. 4, showing some uremic symptoms; discharged improved Mar. 21; creatinine 2.9 and urea N 17 Mar. 1; died about a year later.
91. L. D.	April 7, 1916	56	M.	4.8	28	25	1 yr.	"	Prostatectomy; died a year later; cause of death unknown.
92. W. S.	Mar. 30, 1916	3	M.	4.8	70	. . .	. . .	Recovered	Nephritis following pneumonia and measles; admitted Mar. 28; discharged cured May 18.
93. C. S.	July 9, 1918	69	F.	4.8	122	2	4 days	Dead	Also carcinoma of stomach; CO_2 90; admitted July 6; died July 10.
94. M. McA.	Jan. 25, 1916	44	M.	4.6	71	14-30	1½ yrs.	Recovered	Admitted Jan. 7; positive Wassermann; discharged improved Feb. 3; salivated from Hg. at time of blood examination; CO_2 32, creatinine on May 8, 1917, 2.4 and urea N 16.5; no albumin in urine.
95. O. C.	Oct. 19, 1917	53	M.	4.5	31	0	2 wks.	Dead	Admitted Oct. 9, suprapubic cystotomy for constriction of prostatic urethra Oct. 20; died Oct. 25.
96. A. N.	Aug. 27, 1918	65	M.	4.5	43	. . .	2 days	"	Chronic parenchymatous nephritis and myocarditis; marked unilateral edema; admitted Aug. 9; died Sept. 12; myocardial death.
97. M. R.	Feb. 20, 1917	33	M.	4.4	37	30	6 mos.	"	Admitted Feb. 9; discharged, improved, Feb. 20; died during summer.
98. P. L.	Jan. 24, 1916	47	F.	4.3	28	13	2 wks.	"	Carcinoma of liver; admitted Jan. 9; died Jan. 23.
99. W. C.	Jan. 17, 1916	49	M.	4.1	62	38-52	2½ yrs.	Recovered	Admitted Jan. 15 in coma, apparently due to acidosis; CO_2 combining power 22; alkali therapy; Feb. 1 creatinine 2 and urea 19; left hospital Feb. 15; all right at present time.
100. D. S.	Nov. 14, 1917	64	M.	4.1	86	. . .	1 wk.	Dead	Suprapubic vesical fistula; excision of fistula; admitted Nov. 8; died Nov. 15.

The individual analyses of 3 such cases are given in Tables II, III and IV. Cases 2 (E. M.[27]) and 25 (A. N.) are good illustrations of cases obviously in the last stages of the disease, but who, nevertheless, were able to be up and about. Case 30 (J. B.) was one of the most interesting cases we have encountered. His blood showed a creatinine of 7.5 mg. when he first came under our observation, and although he showed considerable clinical improvement over a period of nearly seven months, still his blood creatinine remained relatively constant. The dietetic measures which were employed to alleviate the nitrogen retention[28] resulted in a gradual reduction of the urea

TABLE II.—INDIVIDUAL OBSERVATIONS ON CASE 2, E. M.

Date, 1915.	Chemical blood analyses.				
	Creatinine. mg. to 100 c.c.	Urea N. mg. to 100 c.c.	Uric acid. mg. to 100 c.c.	Sugar, per cent.	CO_2 combining power, c.c. to 100.
Nov. 30 . .	17.5	97	6.5	0.18	24
Dec. 4 . .	21.5	129	6.4	0.23	21
7 . .	21.8	129	6.3	0.18	23
10 . .	22.3	132	7.0	0.22	20
14 . .	28.9	144	6.1	0.21	24
17 . .	24.2	150	5.6	0.20	15
21 . .	28.6	186	5.0	0.18	18
24 . .	26.7	200	7.7	0.24	12

Patient was up and about on November 30; had stopped in New York on his way to Florida for the winter; systolic blood-pressure 240; phthalein output 0 on three examinations; on December 10 specific gravity of urine continuously 1.005, with 0.25 per cent. NaCl and 0.50 per cent. urea; died on December 25.

TABLE III.—INDIVIDUAL OBSERVATIONS ON CASE 25, A. N.

Date, 1918.	Chemical blood analyses.				
	Creatinine. mg. to 100 c.c.	Urea N. mg. to 100 c.c.	Uric acid. mg. to 100 c.c.	Sugar, per cent.	CO_2 combining power, c.c. to 100.
Mar. 12 . .	8.6	97	8.1	0.181	31
19 . .	9.4	102	7.0	0.131	
22 . .	12.6	110	...	0.120	17
26 . .	12.1	110	...	0.161	28
29 . .	11.9	...	...	0.166	28
April 16 . .	11.2	78	...	0.182	23
30 . .	13.3	81	...	0.152	24
May 7 . .	15.2	76	...	0.200	25
24 . .	17.0	148	...	...	12

Patient discharged clinically improved on March 30, came to laboratory at our request for blood examination on April 16; readmitted to hospital on April 27 and died on May 25.

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[27] For further discussion of this case, see Halsey: Jour. Am. Med. Assn., 1916, lxvi, 1847.

[28] Chace and Rose: Ibid., 1917, lxix, 440.

nitrogen from 135 mg. per 100 c.c. to slightly below 30 during this period. Despite his high creatinine, the patient left the hospital feeling well, returned to work as guard on the subway and did not die until about five months later.

TABLE IV.—INDIVIDUAL OBSERVATIONS ON CASE 30, J. B.

Date, 1916-1917.	Chemical blood analyses.					Phthalein, 2-hour output per cent.
	Creatinine. mg. to 100 c.c.	Urea N. mg. to 100 c.c.	Uric acid. mg. to 100 c.c.	Sugar, per cent.	CO_2 combining power, c.c. to 100.	
Dec. 20 . .	...	...	...	...	...	3
22 . .	7.5	60	...	0.138		
26 . .	7.3	62	...	0.135		
29 . .	...	...	...	...	...	7
Jan. 5 . .	9.7	135	...	0.156	32	
9 . .	12.5	110	...	0.164		
16 . .	9.5	93	...	0.156	49	
23 . .	8.1	57	...	0.144	44	
26 . .	8.2	53	...	0.195		
30 . .	7.8	48	5.0	0.144		
Feb. 2 . .	6.4	50	5.1	0.117		
6 . .	7.8	51	4.2	0.129		
9 . .	8.3	53	5.6	0.171	50	
13 . .	7.8	52	6.4	0.141	51	
16 . .	9.1	56	5.4	0.144		
20 . .	8.3	55	...	0.184		
23 . .	7.9	61	...	0.114	40	
27 . .	7.5	45	7.1	0.120		
Mar. 2 . .	6.6	44	...	0.117	44	
6 . .	6.4	49	6.1	0.123		
9 . .	7.2	50	...	0.126		
13 . .	8.3	50	...	0.135		
16 . .	6.5	37	...	0.108		
20 . .	10.6	53	...	0.140		
23 . .	7.7	40	...	0.117	...	5
27 . .	7.7	44	...	0.126	...	4
30 . .	7.1	46	...	0.123		
April 3 . .	7.2	49	...	0.135		
6 . .	6.9	42	...	0.120		
10 . .	6.2	41	...	0.119		
13 . .	6.4	46	5.9	...		
14 . .	...	...	...	...	...	6
17 . .	6.0	49	...	0.120		
20 . .	6.9	49	...	0.132	...	10
24 . .	6.0	43	...	0.120		
27 . .	7.5	45	...	0.132		
30 . .	...	...	...	...	...	19
May 1 . .	5.9	31	...	0.132		
8 . .	6.6	35	...	0.132		
15 . .	7.3	33	...	0.140		
17 . .	...	...	...	...	...	17
22 . .	7.3	24	...	0.129	...	
June 1 . .	...	...	...	...	...	9
5 . .	6.7	34	...	0.120	...	10
July 17 . .	6.8	29	...	0.152		

Patient kept on low protein diet for five months; discharged from hospital clinically improved on June 9, returned to work as guard on the subway; died November 7, 1917.

Of the remaining 12 cases showing over 5 mg. creatinine, Cases 74 to 85, 8 have died, 2 have apparently recovered, 1 is improved and 1 is unchanged. In view of our statement regarding creatinines of over 5 mg., it is of interest to examine the findings in these 4 cases. Case 74 (F. F.) suffered from acute suppression of urine, but with improvement in the activity of the kidneys the urea nitrogen dropped from 106 to 21 mg. in nine days and the creatinine from 6.1 to 4.2 mg. In Case 75 (J. C.) the creatinine maintained a level of over 5 mg. for not much more than a week, as shown in Table VI. It is interesting to note that a year later the blood presented quite a similar picture, although at this time the creatinine was 4.5 mg.

TABLE V.—INDIVIDUAL OBSERVATIONS ON CASE 74, F. F.

Date, 1917–1918.	Chemical blood analyses.				
	Creatinine. mg. to 100 c.c.	Urea N. mg. to 100 c.c.	Uric acid. mg. to 100 c.c.	Sugar, per cent.	CO_2 combining power, c.c. to 100.
Dec. 18 . .	6.1	106	11.4	0.106	
21 . .	5.9	93	11.2	0.150	54
27 . .	4.2	21	5.0	0.135	
Jan. 2 . .	4.0	23	...	0.096	
4 . .	3.7	26	...	0.090	
8 . .	3.8	28	...	0.122	
Oct. 30 . .	...	10			

Patient admitted to hospital on December 17 following suppression of urine for three days apparently due to an injury; convulsions, edema of face, vomiting four days, rapidly improved and left hospital on January 17; phthalein, December 19, 16 per cent.; December 24, 44 per cent.; December 26, 42 per cent. and January 4, 57 per cent.; apparently well at present time.

TABLE VI.—INDIVIDUAL OBSERVATIONS ON CASE 75, J. C.

Date, 1917.	Chemical blood analyses.				
	Creatinine. mg. to 100 c.c.	Urea N. mg. to 100 c.c.	Uric acid. mg. to 100 c.c.	Sugar, per cent.	CO_2 combining power, c.c. to 100.
April 24 . .	3.8	28	6.8	0.108	
May 19 . .	2.1	35	7.4	0.120	
8 . .	6.1	41	5.5	0.132	50
15 . .	5.2	30	7.7	0.126	
22 . .	3.3	28	7.7	0.120	
June 1 . .	3.1	36	10.4	0.117	
8 . .	4.5	26	...	0.129	
1918.					
April 2 . .	3.8	57	...	0.119	
26 . .	4.5	51	6.7	0.128	
1919.					
Jan. 19 . .	4.3	64	...	0.135	34

Patient in hospital from April 23 to June 10, 1916; phthalein 10 per cent. on April 25, 9 per cent. on May 3 and 7 per cent. on May 22; again in hospital April 1 to May 4, 1918, in rather poor health during October but feeling quite well in January, 1919.

With Case 79 (H. G.) the creatinine remained over 5 mg. for only a very brief period, probably not more than two or three days. A prostatectomy was performed upon Case 83 (R. McC.). On

TABLE VII.—INDIVIDUAL OBSERVATIONS ON CASE 78, H. G.

Date, 1917.	Chemical blood analyses.				
	Creatinine. mg. to 100 c.c.	Urea N. mg. to 100 c.c.	Uric acid. mg. to 100 c.c.	Sugar, per cent.	CO_2 combining power, c.c. to 100.
May 8 . .	4.9	45	9.0	0.140	46
15 . .	3.0	45	...	0.110	
18 . .	4.6	39	...	0.156	
22 . .	3.1	26	...	0.120	
25 . .	2.6	30	...	0.120	
29 . .	5.6	70	...	0.118	
June 1 . .	4.7	60	...	0.117	40
8 . .	3.5	48	...	0.120	
15 . .	2.5	23	...	0.129	
29 . .	3.8	31	...	0.141	
July 13 . .	3.2	26	...	0.120	

Patient admitted on May 2 complaining of pain in umbilical region, loss of weight, anorexia; no nephritic symptoms; phthalein on May 15, 35 per cent., May 18, 24 per cent.; left hospital improved on June 10; apparently well for more than a year past, in army at present time.

TABLE VIII.—INDIVIDUAL OBSERVATIONS ON CASES 94 AND 99.

Date, 1916.	Chemical blood analyses.				
	Creatinine. mg. to 100 c.c.	Urea N. mg. to 100 c.c.	Uric acid. mg. to 100 c.c.	Sugar. per cent.	CO_2 combining power, c.c. to 100.
		CASE 94,	M. McA.		
Jan. 11 . .	3.6	41	4.6	0.110	
25 . .	4.6	71	4.6	0.132	22
April 11 . .	2.7	17	6.3	0.165	45
1917.					
May 9 . .	2.4	17	5.6	0.135	
1916.		CASE	99, W. C.		
Jan. 15 . .	3.5	44	9.5	...	22
17 . .	4.1	62	...	...	58
18 . .	2.0	42	5.6	0.152	56
19 . .	3.2	53	4.3	0.120	54
28 . .	1.9	19	2.5	0.138	
Feb. 1 . .	2.0	19	2.8	0.150	
1918.					
June 11 . .	1.8	16	4.4	0.150	

Case 94 admitted to hospital on January 7, also syphilitic; salivation as result of mercury salicylate given on January 16 and 18; phthalein on January 8, 14 per cent. on January 26, 30 per cent.; left hospital improved on February 3; apparently recovered judging from two subsequent blood examinations.

Case 99 admitted to hospital in coma apparently due to acidosis, obtained almost immediate relief with alkali therapy; use of alcohol important etiological factor; use of alcohol discontinued; perfectly well and blood essentially normal two and a half years later.

November 8, three weeks after the operation, the creatinine was 4.9 and the urea nitrogen 32 mg., essentially the same as on the first examination. One kidney had been removed at a previous operation. After two months the patient still appeared to be doing well clinically. Further discussion of the individual cases would appear to be unnecessary, although the findings on Cases 94 (M. McA.) and 99 (W. C.), may be of interest (Table VIII). These cases apparently completely recovered from the acute condition from which they suffered when admitted to the hospital. From an inspection of Table I it is apparent that the cases with the high creatinine values are for the most part clear-cut cases of interstitial nephritis, while many of the cases at the foot of the list suffered from various other complications.

TABLE IX.—OBSERVATIONS ON A CASE OF PARENCHYMATOUS NEPHRITIS.

Date, 1915-1916.	Chemical blood analyses.					Phthalein, 2-hour output, per cent.
	Creatinine. mg. to 100 c.c.	Urea N. mg. to 100 c.c.	Uric acid. mg. to 100 c.c.	Sugar, per cent.	CO_2 combining power, c.c. to 100.	
Aug. 27 . .	1.9	28	2.3	0.18	...	
29 . .	...	...	...	...	...	8
31 . .	1.9	23	4.0	0.18		
Sept. 24 . .	3.0	25	3.3	0.17		
Oct. 1 . .	2.9	25	2.5	0.14		
25 . .	...	...	...	...	...	24
26 . .	3.0	29	2.8	0.14		
Nov. 11 . .	...	...	...	...	...	19
19 . .	3.5	28	2.4	0.16		
Dec. 3 . .	2.6	25	3.1	0.18		
17 . .	2.8	21	...	0.18		
24 . .	3.6	27	3.0	0.18	54	
29 . .	...	...	...	...	...	4
31 . .	...	...	...	...	56	
Feb. 18 . .	2.7	25	...	0.18		
21 . .	...	...	...	...	...	24
April 4 . .	3.0	28	3.4	0.18		
May 20 . .	3.4	46	8.3	0.15		

J. E. P. admitted on August 25, 1915, complaining of swelling of feet and abdomen and shortness of breath for eighteen months past; constant mild glycosuria of 0.5 per cent.; blood chlorides as NaCl on December 3, 0.73 per cent. and on February 18, 0.7 per cent.; died on June 1, 1916.

General Discussion. The deductions which have been drawn regarding the blood creatinine apply particularly to cases of interstitial nephritis. In such conditions as bichloride poisoning and acute nephritis it is possible to have considerable nitrogen retention with ultimate recovery, for the reason that here the activity of the kidneys is only temporarily depressed. It is scarcely necessary to mention, however, that in comparison with chronic interstitial nephritis these cases are very much less common. In bichloride poisoning it may be noted that Cohen and Bernhard[29] have reported a non-fatal case with a creatinine of 9.3 mg., while in a non-fatal case reported by Campbell[30] the creatinine reached 12.5 mg. Cases 74 and 78 in our series would naturally be classed as cases of acute nephritis.

The changes found in the blood in true cases of parenchymatous nephritis would appear to be quite different. Data on J. E. P., in Table IX, illustrate this point. As will be noted, no marked accumulation of creatinine ever occurred, and there was only a moderate retention of urea even up to the time of death. A detailed history of this case has already been published by Bailey in another connection.[31]

TABLE X.—CASES WITH MARKED UREA RETENTION BUT WITH ESSENTIALLY NORMAL CREATININE VALUES, ALL IMPROVED.

Case.	Date.	Age.	Sex.	Blood analyses.		Phthalein 2-hour output, per cent.	Remarks.
				Creatinine.	Urea N.		
				mg. to 100 c.c.			
1. J. P.	April 23, 1915	34	M.	3.2	72	17	Acute parenchymatous nephritis with edema of extremities and difficult urination, remained in hospital 42 days after this date.
2. L. B.	Aug. 6, 1915	32	F.	3.1	67	..	Pulmonary tuberculosis and acute parenchymatous nephritis; in hospital 92 days.
3. D. B.	Oct. 9, 1917	38	M.	3.1	65	50	Tabes dorsalis and acute nephritis, after week's rest urea N dropped to 15 and phthalein rose to 68.
4. K. K.	Dec. 29, 1916	46	F.	3.4	63	..	Nephrolithiasis, nephrotomy under spinal anesthesia.
5. M. C.	July 18, 1916	11	M.	2.8	60	18	Acute parenchymatous nephritis with generalized edema, in hospital one month.
6. A. M.	July 7, 1916	63	M.	2.3	51	26	Endocarditis and syphilitic aortitis, edema of extremities and dyspnea; in hospital one month.
7. B. S.	Jan. 2, 1918	70	M.	2.6	50	10	Chronic parenchymatous nephritis; left hospital 30 days after this date.
8. M. S.	Dec. 12, 1916	35	M.	2.2	50	..	Duodenal ulcer, alcoholic history; 2 days before leaving hospital phthalein 57 per cent.
9. H. P.	Mar. 5, 1918	32	M.	2.4	50	..	Pleural effusions; tuberculous kidney removed 1 year ago.
10. R. K.	Feb. 2, 1918	11	F.	2.5	50	..	Acute uremia, anuria; after 3 days phthalein 32 per cent.

Inasmuch as the blood urea and the phenolsulphonephthalein test on the urine are likewise recorded in parallel columns in Table I, it affords an opportunity to compare the value of these three tests. As pointed out in the introductory portion of the paper the blood urea is subject to much greater fluctuation than the creatinine, due largely to the difference in its origin. Since the urea is a more sensitive indicator of renal impairment it is particularly useful as a diagnostic test in medical cases[32] or as a pre-operative prognostic test in surgical cases,[33] but much less valuable than the creatinine as a prognostic test in cases of advanced nephritis. That a considerable accumulation of urea may occur without a retention of cretinine, but with ultimate improvement in the condition of the patient, is evident from the data presented in Table X. An accumulation of non-protein and urea nitrogen occurs in acute intestinal obstruction,[34] but an accumulation of creatinine should not occur unless the kidneys are involved. All these facts lead to the conclusion that the accumulation of urea possesses a somewhat different significance from that of creatinine.

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[29] Jour. Am. Med. Assn., 1917, lxix, 440.

[30] Arch. Int. Med., 1917, xx, 919.

[31] Bailey: Am. Jour. Med. Sc., 1919, clvii, 221.

The results on the phthalein test recorded in Table I speak well for the prognostic value of this test. They agree excellently with the creatinine in the prognosis indicated, and in one or two instances the information appears to have been especially significant. Case 30 is the most notable illustration. Here there was an appreciable output of phthalein for some time, and the case survived much longer than any other with a similar creatinine retention. As has been pointed out by Frothingham, Fitz, Folin and Denis,[35] however, there is this difference between the phthalein and the blood tests: The phthalein test shows the renal function at the moment, while the blood tests (they used the non-protein and urea nitrogen) are rather a measure of the accumulating difference between the amounts of waste nitrogen produced in metabolism and the amounts eliminated by the kidney. In an acute condition a negative phthalein might be encountered without a marked creatinine retention. In advanced cases of nephritis, on the other hand, changes in condition are accompanied by changes in the blood creatinine, but obviously there can be no change in a negative phthalein. The blood creatinine and urea and the phthalein test excellently supplement each other in indicating the extent and type of impairment of renal function, and where possible, use should be made of all three tests. From the standpoint of prognosis, however, we believe the creatinine gives the most reliable information, and in cases beyond medical help, such as the majority of those listed in Table I, this is the factor of greatest importance.

Data on the presence of protein and casts in the urine of the cases in Table I have been intentionally omitted. In passing, it should perhaps be noted that several of the very severe cases failed to show either protein or casts in the urine.

[32] Kast and Wardell: Arch. Int. Med., 1918, xxii, 581.

[33] Squier and Myers: Jour. Urol., 1918, ii, 1.

[34] Tileston and Comfort: Arch. Int. Med., 1914, xiv, 621; Whipple and Van Slyke: Jour. Exper. Med., 1918, xxviii, 213.

[35] Arch. Int. Med., 1913, xii, 245.

SUMMARY. Observations are recorded on 100 cases of nephritis showing creatinine retention. Of these 100 cases, 85 had a creatinine of over 5 mg. per 100 c.c. of blood, the figures ranging from 5.1 to 33.3 mg.; 80 of these 85 cases have died. Of the 5 remaining the condition of 3 is essentially unchanged, while 2 have recovered. These 2 cases showed only a temporary elevation of the blood creatinine.

A considerable number of the 85 cases were able to be up and about and some showed decided clinical improvement. The creatinine gave us a better prognostic insight into these cases than either the blood urea or phthalein tests, which were made simultaneously. It is our opinion that in advanced cases of nephritis the blood creatinine furnishes a more reliable prognosis than any other test we possess.

REMARKS ON OCULOGYRATION AND ON THE LESION CAUSING COMPLETE BILATERAL OPHTHALMOPLEGIA.[1]

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FRENCH neurologists employ the term *oculogyre* and its various modifications. In seeking English equivalents for these terms I have consulted the *Standard Dictionary*, as I am informed by certain ophthalmologists with whom I have conferred that the French usage is not common in American ophthalmology. A gyre may mean a gyration, it may also mean a gyrus, as one of the convolutions of the brain. Gyration means: "The act of turning, as a body on its axis of rotation, while simultaneously whirling about an axis of revolution," and it seems better adapted to the translation than gyre. I have employed the terms dextrogyration and sinistrogyration to mean right lateral associated movement of the eyeballs and left lateral associated movement, respectively.

The attempt is made in this paper to discuss certain aspects of oculogyration and to distinguish clinically between lesions above and below the nucleus of the branch of the oculomotor nerve supplying the internal rectus muscle, causing disturbance of lateral associated ocular movement; also to explain the lesion causing complete bilateral ophthalmoplegia in a way I have not seen employed in literature. A lesion at a considerable distance above the oculomotor nucleus probably could not cause persistent paralysis of ocular movements, as such movements are bilaterally represented in the cerebral cortex.

G. S., aged fifty-two years, was admitted to the University Hos-

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[1] Read before the Philadelphia Neurological Society, February 28, 1919.